

*A2 Amend* <sup>47</sup> 48. (NEW) A method according to claim <sup>46</sup> 47 wherein the drop dispensers are pulse jets.

Remarks

As a preliminary matter, the Examiner is thanked for the acknowledgment of the Supplemental IDS filed Nov. 20, 1999. However, Applicants have not received any acknowledgement of the original IDS filed on April 30, 1999 with the present application.

The Examiner is also thanked for the Action of July 18, 2000 (request for a 1-month extension to respond, enclosed), and the allowance of claim 18 and indicated allowability of claims 4, 14-17, 20-24, 28, and 32-38. The Examiner rejected claims 1-3, 5-13, 25-27, 29-31, 39, 40 under 35 U.S.C. 103(a) as being unpatentable over McGall (US 5,843,655). This rejection is discussed below with regard to the indicated claim.

Claim 37, which was indicated as allowable, was previously dependent on claim 35 through claim 36. Claim 37 continues to reference evaluating the dispenser or fluid as being responsible for an error, however claim 35 only references evaluating if a dispenser was responsible. Thus, claim 37 has been amended to make it dependent upon claim 25 with the added limitations being taken from the language of claim 35. It is therefore believed that claim 37 should continue to be allowable. New claims 43 (and apparatus claim 46) contain many of the similar limitations as claim 23, although in claims 43, 46 the control processor operates the multiple dispensers to correct for the identified error (and specifically on the same array in claims 43, 47, and where the dispensers are pulse jets in claims 47, 48). Such operation for correction is disclosed, for example, in page 4, line 29 to page 5, line 23.

The rejection of claims 1-3, 5-13, 25-27, 29-31, 39, 40 under 35 U.S.C. 103(a) is discussed below.

Claims 1-3, 5-13, 25-27, 29-31

In the rejection, the Examiner took the position that McGall column 11, line 20 and through the Examples, discloses "optical reading of labels, etc. on the array surface for manufacturing evaluation". The Examiner further noted that images in McGall were stored in a computer (referencing column 12, lines 65-67).

As the Examiner is aware, he has the initial burden of establishing a *prima facie* case of obviousness:

"In rejecting claims under 35 USC § 103, the examiner bears the initial burden of presenting a *prima facie* case of obviousness. (citations omitted) Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant." (In re Rijckaert 28 USPQ2d 1955 (Fed. Cir. 1993) @ 1956)

The Examiner can satisfy this burden by pointing to a suggestion or motivation in the prior art which leads to the claimed invention, without the benefit of hindsight.

In the present case, the Examiner relies on the referenced portions of McGall and concludes that they are "deemed to motivate and suggest the comparison between the target or desired pattern...and what actually has been fabricated". However, the Examiner has not pointed to anything in the prior art (McGall) that suggests comparing an actual pattern obtained with the target pattern. For this reason alone, the rejection based on McGall should be withdrawn.

In addition though, if anything, McGall suggests that any comparison for manufacturing quality of data from the actual fabricated array, is done within the actually deposited array data itself. In particular, McGall simply evaluates how much of a given type of oligonucleotide is present on the actually deposited array only, after exposure to a test condition. This is made clear in Section II, column 6, lines 14-26:

"A general method of this invention is directed to determining the extent to which a test condition causes the appearance of a structural feature in oligonucleotides produced on an oligonucleotide array by spatially directed oligonucleotide synthesis. This method involves providing a substrate having a surface with linkers having an active site for oligonucleotide synthesis. An ensemble of sequence-specific oligonucleotides is synthesized on the substrate by spatially directed oligonucleotide synthesis. The oligonucleotides can be provided with active sites for attaching a detectable label. **The area is exposed to the test condition. Then, the amount of oligonucleotides having the structural feature is determined**" (emphasis added)

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Similarly, in Section III dealing with the particular situation of a structural feature in the form of coupling efficiency (beginning on col. 6, line 27), the end evaluation is made by comparing different areas within the actually deposited array:

**"After at least two rounds of nucleotide coupling, the chip can be tested for coupling efficiency. This testing involves determining the amounts of competent, uncapped active sites in any two areas of the substrate. Then, the amounts are compared, thereby providing the efficiency of nucleotide coupling between the two areas."** (emphasis added) (col. 7, lines 4-9).

Again in section IV dealing with deprotection efficiency (beginning on col. 8, line 50) the end evaluation is made simply by evaluating characteristics of the array actually deposited (without any reference to the target pattern):

**"After exposure to the test condition, the substrate is washed, exposing any unprotected active sites ("OH") on nucleotides from which the protective group has been removed (710). The amount of unprotected active sites is determined in the area. The amount indicates the extent to which the test condition caused removal of protective groups."** (emphasis added) (col. 8, line 65 to col. 9, line 4)

In section V dealing with rates of depurination (beginning col. 9, line 21) there is also no comparison with the target array:

**"The amount of uncleaved oligonucleotides in the area is determined, preferably by imaging of the surface tag. This reveals depurination by a reduction in surface tag in the regions subjected to the test conditions relative to that elsewhere on the surface. The amount of depurination is inversely related to the amount of detectable label coupled to an ensemble."** (col. 9, lines 61-67)

Once again in section VI dealing with a structural feature in the form of formation of double-stranded structures (beginning at col. 6, line 35) there is no comparison with a target pattern in order to obtain the desired reading:

**"This releases from the substrate label attached to cleaved, double-stranded structures, leaving only label on uncleaved oligonucleotides (1110). Then, the amount of detectable label in the area is determined. The amount of label is inversely related to the amount of double-stranded structures in the area."** (col. 11, lines 14-19).

Thus, as seen from the above McGill makes use of data from only within the array actually formed, and does not suggest for any reason that one should compare such data with the target array pattern. The Examiner references optical reading of labels in McGill beginning at column 11, line 20. However, that entire section merely

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discloses conventional scanning of an array in order to obtain data which is used to evaluate the extent of formation of the structural feature of interest (as described in section II mentioned above, and those specific types of structural features of sections III through VI). As shown above, the evaluation of such structural features is done solely within data from the actually formed array, and nothing in the relied upon section beginning in column 11 suggests anything different.

Thus, not only has the Examiner not pointed to anything in McGall which might suggest comparing the actual pattern with the target pattern, as recited in claim 1, but McGall itself in fact suggests that the only comparison to be done is within data obtained from the actually deposited array itself.

For the foregoing additional reason, the rejection of claims 1 and 25 (and claims 2, 3, 5-3, 26, 27, 29-31 which are directly or indirectly dependent thereon) should now be withdrawn.

As an additional point, it should be noted that even if it might be argued one might have adapted McGall so that the data obtained from the actually deposited actual array could have been compared to the target array, it is well settled that the possibility that the prior art may be modified so as to produce a claimed invention does not amount to obviousness:

"The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification" (citation omitted) (*In re Fritch* 23 USPQ2d 1780 (Fed.Cir. 1992) @ 1783-1784)

Furthermore, even if McGall had said nothing about what was to be done with the collected data (contrary to what has been pointed out above) this would only leave the situation where the use of such data from the actually deposited array would be unknown. The Examiner could still not presume, even assuming this hypothetical situation in McGall, that there is therefore a suggestion that such data would have been used in a claimed method. This has been pointed out by the Federal Circuit in *In re Grasselli*, 218 USPQ 769 at 765 (Fed. Cir. 1983):

"If appellant's catalyst is inherent in the Japanese Patent, it has not been established by the record here and obviousness cannot be predicated on that which is unknown." (emphasis added)

Claims 39-41

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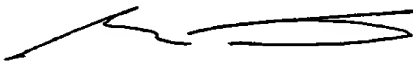
With regard to claim 39 (and 40, which is dependent thereon), that claim recites among other features that "the imaging system includes a light receiving element mounted for movement by the transporter". The Examiner has not pointed to any such suggestion in the prior art and accordingly claims 39, 40 should now be allowed for at least this reason.

With regard to new claims 41, this adds the limitation that the actual pattern is compared with the target pattern for spot location, dimension or presence, and the method additionally comprising generating a signal indicative of the result of the comparison. New claim 42 adds similar apparatus features. These features are described, for example, on page 4, lines 5-13 of the present application (and page 14, lines 21-24 for the apparatus). The Examiner has not pointed to any such features in McGall and claims 41, 42 should therefore be allowed for this additional reason.

#### Summary

In view of the above, it is submitted that claims 1-3, 5-13, 25-27, 29-31, 39 and 40 should also now be in condition for allowance. If the Examiner is of the view that there are any outstanding issues, he is invited to call Gordon Stewart at (650)485-2386.

Respectfully submitted,



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